In claims 1 and 39, the compound of Formula (I) has been added, and is supported by the specification at, for example, page 6, lines 10-15. Claim 39 has also been editorially amended and is supported by the specification at, for example, page 15, lines 11-19.

Claim 17 has been editorially amended and is supported by the specification at, for example, page 12, line 19 to page 13, line 1; and page 14, lines 12-16.

Claims 18, 19, 20, 33 and 35 have been editorially amended to include "black patient."

Added claims 42 and 44 are supported by the specification at, for example, page 5, lines 13-18. Added claims 43 and 45-47 are supported by the specification at, for example, page 25, lines 10-24. Added claim 46 is supported by original claim 2; and claims 47 and 52 by original claim 3. Added claims 48-50 are supported by the specification at, for example, page 15, lines 11-19; page 17, lines 9-15; page 25, lines 19-24; Figs. 2A-2B; and original claims 1, 3, 6 and 10.

No issues of new mater should arise and entry of the amendment is respectfully requested.

II. Rejection under 35 U.S.C. § 103

Claims 1-41 are rejected under 35 U.S.C. § 103 as being obvious over Cohn (U.S. Patent No. 4,868,179).

Applicants respectfully traverse the rejection and respectfully submit that Cohn does not disclose or suggest the presently claimed invention.

In the examples in the specification at pages 15-25 and Figures 2A-2B, Applicants have demonstrated that the claimed methods for administering a hydralazine compound of Formula (I) or a pharmaceutically acceptable salt thereof and at least one of isosorbide dinitrate and isosorbide mononitrate produces unexpectedly superior results in the treatment of black patients when compared to white patients. Cohn does not provide any evidence or suggestion that the combination of claimed compounds would provide unexpectedly superior results in treating a black patient. MPEP § 716.02

For example, the results demonstrate that the claimed methods for administering a hydralazine compound of Formula (I) or a pharmaceutically acceptable salt thereof and at least one of isosorbide dinitrate and isosorbide mononitrate resulted in an unexpectedly reduced mortality rate from heart failure in the treatment of black patients when compared to white

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patients. *See* Specification at page 5, lines 2-4; page 18, lines 1-21; Figs. 2A and 2B. The difference in mortality from heart failure between black patients and white patients was statistically significant. *See* specification at page 5, lines 2-5; and page 18, lines 16-21. For the Examiner's convenience Figures 2A and 2B from the specification are shown below.

Figure 2A

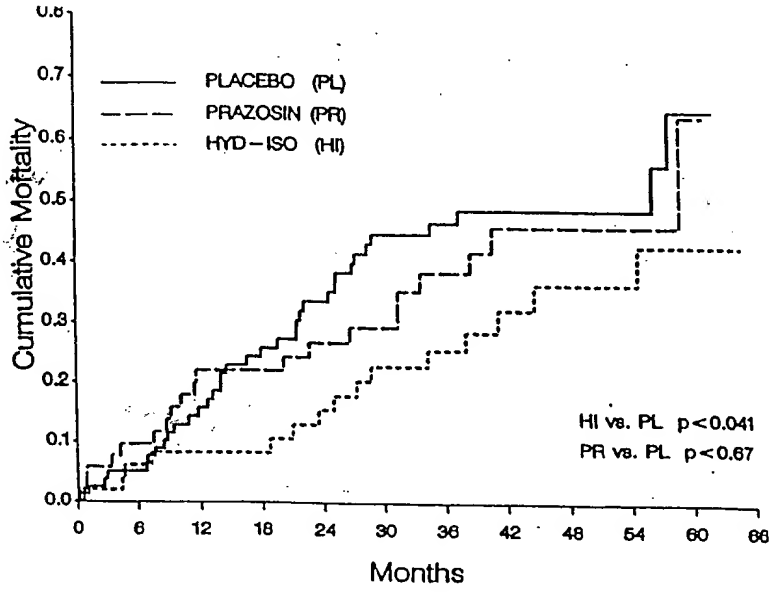

Figure 2B

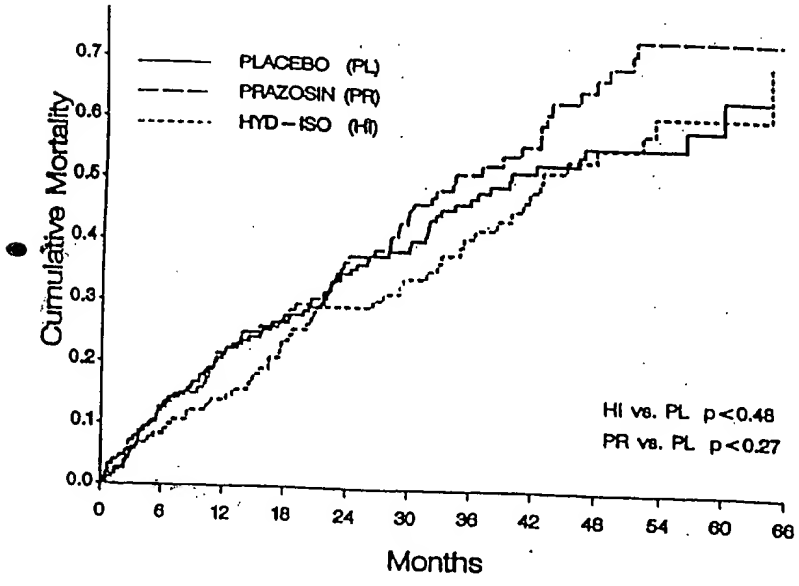

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Figure 2A in the specification shows that administering hydralazine and isosorbide dinitrate to black patients unexpectedly reduced mortality in a manner superior to the administration of placebo or prazosin (e.g., an angiotensin converting enzyme (ACE) inhibitor). Figure 2B in the specification shows that white patients, unlike black patients, did not respond favorably when treated with hydralazine and isosorbide dinitrate. Again, the results in the specification, as set forth in Figs. 2A and 2B, show that the claimed combination of hydralazine and isosorbide dinitrate provides unexpectedly superior results when administered to black patients when compared to the results of the same drugs administered to white patients. The unexpectedly superior results of the present invention are not suggested by Cohn.

Furthermore, nothing in Cohn would motivate one to administer hydralazine and isosorbide dinitrate to a black patient who is not as responsive to an angiotensin-converting enzyme inhibitors relative to a white patient; who has hypertension; who has a deficient nitric oxide generating system; and/or who has a less active renin-angiotensin system relative to a white person.

Again, Cohn does not disclose or suggest that administering the combination of a hydralazine compound of Formula (I) and isosorbide dinitrate or isosorbide mononitrate to black patients would result in an unexpectedly superior reduced mortality (specification at Figs. 2A and 2B; page 5, lines 2-4; page 18, lines 1-21), an unexpectedly superior improvement in oxygen consumption (specification at page 19, line 28 to page 21, line 1); an unexpectedly superior improvement in quality of life (specification at page 20, lines 14-19); or an unexpectedly superior improvement in exercise tolerance (specification at page 19, line 28 to page 21, line 1).

In view of the above, Applicants respectfully submit that the presently claimed invention is unobvious over Cohn, and respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

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